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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,196	01/24/2002	Y. Tom Tang	039386-0220	3875

22428 7590 07/31/2006

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 07/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/744,196	Applicant(s) TANG ET AL.	
	Examiner Stacy B. Chen	Art Unit 1648	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 July 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: 3-11.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of Item 5. Applicant's reply has overcome the following rejection(s): The rejection of claims 3-11 under 35 U.S.C. 112, second paragraph, as indefinite, is withdrawn in view of Applicant's amendment.

Continuation of Item 7. Applicant's after-final amendment filed July 17, 2006 is acknowledged and entered. Claims 3-11 are pending and under examination.

The rejection of claims 3-11 under 35 U.S.C. 101 for not being supported by either a specific, substantial and credible asserted utility, or a well established utility, is maintained for reasons of record. Applicant's arguments filed July 17, 2006 have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

Applicant argues that the claimed invention is supported by an asserted utility. Applicant asserts that the polynucleotides of the claimed invention are associated with cell proliferation. In response to this argument, the Office acknowledges and has acknowledged previously that the claimed invention has an asserted utility.

Applicant argues that the asserted utility is substantial and credible. Applicant points to post-filing evidence to substantiate a substantial and credible utility utility, Wissmann et al., (J. Pathology, 201:204-212), of record. Applicant points out that Wissmann recognizes a substantial utility for the polynucleotide encoding MACP-2 by showing that MACP-2 is down-regulated at the RNA level in 64% of primary prostate cancers. Applicant also argues that this is evidence of a credible utility because it was tested and confirmed by Wissmann. In response to this argument, the examiner has considered the Wissmann reference. Wissmann teaches that MACP-2 (WIF1) was down-regulated in 64% of primary prostate cancers (abstract). Wissmann also teaches that there is no correlation between WIF1 down-regulation and tumor stage or grade for prostate, breast or non-small cell lung carcinomas. Wissmann concludes that WIF1 expression may be an early event in tumorigenesis. Applicant asserts that Wissmann reports on a differential gene expression analysis of particular genes in prostate cancer. Applicant asserts that Wissmann defines differential expression as requiring that the gene must (1) be expressed in at least 50% of prostate tumor patients, (2) be up-regulated or down-regulated in at least 10% of tumor samples, and (3) the degree of up- or down-regulation should be at least two-fold (page 208, col. 1, second paragraph). Applicant asserts that Wissmann further shows that expression of the polynucleotide encoding MACP-2 is down-regulated at the RNA level in 64% of MACP-2-expressing tumors (page 208, col. 1, third and fifth paragraphs). Applicant argues that these data are consistent with the disclosure of the present application which indicates that MACP-2 is associated with cell proliferative disorders.

In response to Applicant's arguments, the Office has considered the factors that Wissmann uses to determine differential gene expression of particular genes in prostate cancer. With regard to the first factor, the instantly claimed polynucleotide has not been demonstrated as expressed in at least 50% of prostate tumor patients. While the Tables 1, 3 and 4 of the instant specification disclose that MACP-2 is associated with prostate cancer, and that MACP-2 nucleotide is found in 71.4% of cDNA libraries that are proliferative in nature, this is not sufficient to support the conclusion that the instantly claimed gene(s) is expressed in at least 50% of prostate tumor patients. The cDNA libraries were not specific to prostate tumor samples. With regard to the second and third factors, Applicant has not demonstrated that the claimed genes are up-regulated or down-regulated in at least 10% of tumor samples, nor that the genes are up- or down-regulated at least two-fold. It is unclear what population of tumor samples Wissmann is referring to. Regardless, Wissmann shows that the polynucleotide encoding MACP-2 is down-regulated at the RNA level in 64% of MACP-2-expressing tumors. This is not indicative of the second factor, namely, Wissmann only measured down-regulation in tumors that are already known to express MACP-2. The second factor requires that the gene be up- or down-regulated in 10% of tumors, not just the tumors that were pre-selected because of the expression of MACP-2. Wissmann's teachings about MACP-2 are also not indicative of the third factor because the population that Wissmann used to demonstrate 64% down-regulation was only in tumor samples expressing MACP-2, instead of tumor samples generally.

In summary, the claims polynucleotides with the claimed function are not supported by the specification. The differential gene analysis of Wissmann has not been adequately met by Applicant's work or that of Wissmann's with regard to SEQ ID NO: 2 and 7. Therefore, the claims remain rejected for lack of utility.

Claims 3-11 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility, or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The rejection of claims 3-11 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is maintained for reasons of record. The polynucleotide sequences encode polypeptides that are associated with cell proliferation, a utility for which Applicant is not entitled (see rejections above). Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily drawn to the following:

Applicant points to the USPTO's "Synopsis of Application of Written Description Guidelines", Example 14, where a single species was deemed representative of the genus because (1) all members have at least 95% structural identity with the reference sequence, and (2) because of the presence of the assay which applicant provided for identifying all of the at least 95% identical variants which have the specified function. Applicant argues that with regard to the second criteria, one of skill in the art can make the variants and then use Northern blot or microarray analysis of proliferating cells or cells exhibiting proliferative disorder (compared to normal cells). Applicant argues that differential expression of proliferating cells would indicate an association with cell proliferation, as in Examples IV and VII. In response to Applicant's amendment and argument, Applicant has met the first criteria because the claims now recite, "at least 95%" sequence identity. However, with regard to the second criteria, Applicant has not provided a specific function because cell proliferation activity is a diverse genus of activities, of which Applicant has not identified as specific activity to SEQ ID NO: 2 and its variants. The function of the variant polypeptide in Example 14 of the Written Description Guidelines has a specific enzymatic activity, as opposed

to the instantly claimed polypeptides whose cell proliferation activity is not known. The only adequately described species is a polypeptide comprising SEQ ID NO: 2, and a polynucleotide comprising SEQ ID NO: 7. No active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

Stacy B Chen 7/27/04

STACY B. CHEN
PRIMARY EXAMINER